

AMENDMENTS TO THE CLAIMS:

Please cancel claim 2 without prejudice or disclaimer.

Please substitute currently amended claims 1, 3, 13, 50, 53, 55 and 59 for the original or previously presented claims having the same claim numbers.

1. (currently amended) A method for disrupting survival signaling from the microenvironment to cancer cells, said method comprising administering an agent effective in blocking the interaction of an integrin with an extracellular matrix protein of the microenvironment or that downregulates expression of said integrin, wherein the method results in sensitizing cells to chemotherapy, biological therapies or radiation therapy of primary tumors, cancer metastases or micrometastases and hyperproliferative disorders in a mammal.

2. (canceled)

3. (currently amended) The method of claim 1, wherein the integrin is ~~selected from the group consisting of alpha 5 and beta 1 integrin~~ and wherein the extracellular matrix protein is fibronectin.

4. (previously presented) The method of claim 1, wherein the cancer cell is a breast cancer cell or a prostate cancer cell.

5. (previously presented) The method of claim 1, wherein the agent is selected from the group consisting of an antibody specific for an integrin, a blocking peptide, and a modified peptide effective to disrupt interaction of the integrin with the extracellular matrix.

6. (canceled)

7. (previously presented) The method of claim 1, wherein the agent is all trans retinoic acid or a retinoic acid derivative.
8. (previously presented) The method of claim 1, wherein the agent is a kinase inhibitor or a transcription inhibitor.
9. (previously presented) The method of claim 1, wherein the method comprises blocking survival signaling initiated by ligation of integrins by microenvironment proteins.
10. (previously presented) The method of claim 1, wherein the agent is an inhibitor of a kinase, said kinase selected from the group consisting of MEP/MAP kinase, p38, RhoA, Rho kinase, PI3 kinase, PKC, and PKA.
11. (previously presented) The method of claim 10, wherein the inhibitor is selected from the group consisting of LY294002, UO 126, AG82, Y27632, SB203580, PD169316, PD98059, RO318220, and a C3 transferase inhibitor.
12. (previously presented) A method of inhibiting cellular proliferation or inducing cell death or cellular differentiation or for treating a cancer or a hyperproliferative disorders in a mammal comprising administering an agent capable of downregulating expression of an integrin or blocking the binding of an integrin to an extracellular matrix protein.
13. (currently amended) The method of claim 12, wherein the integrin is ~~selected from the group consisting of~~ alpha 5 and beta 1 and wherein the extracellular matrix protein is fibronectin.

Claims 14-46 (canceled)

47. (previously presented) The method of claim 12, wherein the agent is a kinase inhibitor or a transcription inhibitor, and wherein the kinase inhibitor or transcription inhibitor is administered prior to, or concurrent with chemotherapy or radiation therapy.

48. (canceled)

49. (previously presented) The method of claim 12, wherein the cancer is selected from the group consisting of breast cancer and prostate cancer.

50. (currently amended) The method of claim 47, wherein the kinase inhibitor or transcription inhibitor downregulates expression of alpha 5 beta 1 integrins ~~or beta 1 integrins~~ or phosphorylation of Akt.

51. (previously presented) The method of claim 47, wherein the kinase or transcription inhibitor is selected from the group consisting of inhibitors of MEP/MAP kinase, p38, RhoA, Rho kinase, PI3 kinase, PKC, and PKA.

52. (previously presented) The method of claim 51, wherein the inhibitor is selected from the group consisting of LY294002, UO 126, AG82, Y27632, SB203580, PD169316, PD98059, RO318220, and a 3 transferase inhibitor.

53. (currently amended) The method of claim 12, comprising administering an antibody effective to block integrin alpha 5 ~~or~~ beta 1 or a peptide effective to block fibronectin or a modified peptide effective to block fibronectin, or any combinations thereof, wherein the antibody or peptide is administered prior to or concurrent with a chemotherapeutic agent or radiation therapy.

54. (previously presented) The method of claim 50, wherein the method results in sensitizing to, or potentiating chemotherapy or radiation therapy in mammals undergoing treatment for a cancer or a hyperproliferative disorder.

55. (currently amended) A pharmaceutical composition comprising an agent capable of downregulating expression of alpha 5 ~~and/or~~ beta 1 integrins or capable of inhibiting the binding of the integrins to the extracellular matrix, and a pharmaceutically acceptable carrier.

56. (previously presented) The composition of claim 55, wherein the agent is selected from the group consisting of a kinase inhibitor and a transcription inhibitor.

57. (previously presented) The composition of claim 56, wherein the kinase or transcription inhibitor is selected from the group consisting of inhibitors of MEP/MAP kinase, p38, RhoA, Rho kinase, PI3 kinase, PKC, and PKA.

58. (previously presented) The composition of claim 57, wherein the inhibitor is selected from the group consisting of LY294002, UO 126, AG82, Y27632, SB203580, PD169316, PD98059, RO318220, and a 3 transferase inhibitor.

59. (currently amended) The composition of claim 55, wherein the agent is selected from the group consisting of an antibody effective to block integrin alpha 5 ~~or~~ beta 1, a peptide effective to block fibronectin, a modified peptide effective to block fibronectin, and any combinations thereof, wherein the antibody or peptide is administered prior to or concurrent with a chemotherapeutic agent or radiation therapy.